

Richard A. Carnevale
Vice President, Regulatory, Scientific & International Affairs

August 16, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, Maryland 20852

Re: Docket No. 99D-2248 International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH); Draft Guidances on Efficacy of Anthelmintics: General Recommendations (#90), Efficacy of Anthelmintics: Specific Recommendations for Bovines (#95), Efficacy of Anthelmintics: Specific Recommendations for Ovines (#96), and Efficacy of Anthelmintics: Specific Recommendations for Caprines (#97)

The Animal Health Institute (AHI) submits these comments in response to the July 16, 1999 *Federal Register* Notice; request for comments, "International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH); Draft Guidances on Efficacy of Anthelmintics."

AHI is a national trade association representing manufacturers of animal health products – pharmaceuticals, vaccines and feed additives used in modern food production, and the medicines that keep pets healthy.

The Animal Health Institute wishes to commend the Center for Veterinary Medicine for embracing the VICH process and committing resources to the effort to harmonize the technical requirements for product registration. AHI offers the following specific recommendations to bring the efficacy requirements in step with the advances made through the passage of the Animal Drug Availability Act of 1996.

With the inclusion of these recommended changes, AHI encourages CVM to endorse and adopt the VICH draft guidances for anthelmintics. [For ease of reading, words to be deleted have a line through them, and words to be added are underlined.]

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A.4.4. Pooling Data (first paragraph, fourth sentence)

The total number of studies conducted for dose confirmation and persistency needs to include 12 adequately infected control animals i.e., 6 animals in at least 2 trials and an equal number...

B.1. Dose Determination Studies (first paragraph)

Dose titration trials should from now on be referred to as dose determination studies, their purpose being to determine the dose rate to be recommended for the particular target animal. The studies may or may not be conducted using the final formulation. However, if not, any changes in the formulation must be scientifically justified. In some cases, a dose determination study may not be necessary, if there are other arguments that can support the use dose.

B.1. Dose Determination Studies (fourth paragraph)

A commonly used design includes a A minimum of three groups receiving different levels of anthelmintic treatment together with a group of untreated controls should be included in the trials e.g., 0, 0.5, 1 and 2x the anticipated dose. Other trial designs should be agreed with the respective regulatory authority. It is suggested that the range of doses should....

B.2. Dose Confirmation Studies (second paragraph)

At least two controlled or, when appropriate, critical dose confirmation studies per individual claim are recommended (single and multiple infections). Two studies are the minimum needed to verify that efficacy can be achieved against various helminth strains in animals raised in disparate geographic locations and climates and under respective husbandry conditions. At least one of the two studies should be conducted in the region where registration is being pursued and both ~~These~~ studies should be conducted under conditions that are sufficiently representative of the various conditions under which the product will be authorised. In the event that in certain locations parasites are particularly rare then two trials from outside the location will be acceptable. Since the sensitivity of the parasites to treatment should be independent of the geographical location, additional confirmation studies from local regions are not justifiable. Such considerations shall be addressed in the confirmatory field trials. A dose determination study can be used in place of one of the confirmation studies, is the final formulation was used and administered under label recommendations.

B.4. Persistent Efficacy Studies (second paragraph)

As described for dose confirmation, a A minimum for a persistence claim (for each duration and parasite claim)....

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The Animal Health Institute is pleased to submit these comments and looks forward to working closely with representatives from FDA's Center for Veterinary Medicine in the ongoing efforts to harmonize the technical requirements for the registration of veterinary products.

Sincerely,

A handwritten signature in black ink, appearing to read "Richard A. Carnevale", with a long horizontal flourish extending to the right.

Richard A. Carnevale